CURRICULUM VITAE

Jonathan Robert **SECKL** BSc, MBBS, MRCP (UK), PhD, FRCPE, FMedSci

AWARDS, PRIZES AND FELLOWSHIPS

1978 Filliter Prize (1st in Pathology and Microbiology MB).
1980 Hons Viva (Medicine).
1980 Magrath Scholarship/Fellowes Gold Medal (Medicine MB).
1980 The Achison Exhibition (Medicine).
1984 Sir Jules Thorn Trust Research Fellowship.
1989 Wellcome Trust/Royal Society of Edinburgh Senior Clinical Research Fellowship.
1993 Wellcome Trust Senior Research Clinical Fellowship Renewal
1993 FRCP Edin
1994 Norage Pharmacia Prize (best paper on brain aging)
1998 Society for Endocrinology Medal
1999 Mortyn Jones Memorial Lecturer
1999 Fellowship, Academy of Medical Sciences

PRESENT APPOINTMENTS

1997 Moncrieff-Arnott Professor of Molecular Medicine, University of Edinburgh.
1995 Chairman, Molecular Medicine Centre, University of Edinburgh.
1989 Honorary Consultant Physician (Endocrinology), Western General Hospital.

PREVIOUS APPOINTMENTS

1996-97 Professor of Endocrinology, University of Edinburgh.
1993-96 Senior Lecturer in Medicine, University of Edinburgh.
1989-97 Wellcome Trust/Royal Society of Edinburgh Senior Clinical Research Fellow.
1987-92 Visiting Scientist, MRC Brain Metabolism Unit, Edinburgh.
1987-89 University of Edinburgh, Department of Medicine, Lecturer in Medicine
1984-87 Charing Cross and Westminster Medical School,Research Fellow Neuroendocrinology.

EDITORIAL BOARDS

Endocrinology (US); Steroids (US); Journal of Neuroendocrinology; Journal of Endocrinology

KEY RELEVANT PRIMARY PUBLICATIONS IN PEER-REVIEWED JOURNALS (OF 155)

Moisan M-P, **Seckl JR** and Edwards CRW (1990). 11ß-hydroxysteroid dehydrogenase mRNA expression and activity in rat hypothalamus, hippocampus and cortex. *Endocrinology* 127: 1450-1455.

Moisan M-P, **Seckl JR**, Brett LP, Monder C, Agarwal AK, White PC and Edwards CRW (1990). 11ß-hydroxysteroid dehydrogenase mRNA expression, bioactivity and immunoreact-ivity in rat cerebellum. *J Neuroendocrinol* 2: 853-858.

Moisan M-P, Edwards CRW and **Seckl JR** (1992). Ontogeny of 11ß-hydroxysteroid dehydrogenase bioactivity and messenger RNA expression in rat brain and kidney. *Endocrinology* 130: 400-404.

Moisan M-P, Edwards CRW and **Seckl JR** (1992). Differential promoter usage by the rat 11ß-hydroxysteroid dehydrogenase gene. *Molecular Endocrinol* 6: 1082-1087.

Seckl JR, French KL, O'Donnell D, Meaney MJ, Yates C and Fink G (1993). Glucocorticoid receptor gene expression is unaltered in hippocampal neurons in Alzheimer's disease. *Molec Brain Res* 18: 239-245.

Benediktsson R, Lindsay R, Noble J, **Seckl JR** and Edwards CRW (1993). Glucocorticoid exposure in utero: a new model for adult hypertension. *Lancet* 341: 339-341.

Edwards CRW, Benediktsson R, Lindsay R and **Seckl JR** (1993). Dysfunction of the placental glucocorticoid barrier: a link between fetal environment and adult hypertension? *Lancet* 341: 355-357.

Brown RW, Chapman, KE, Edwards CRW and **Seckl JR** (1993). Human placental 11ß-hydroxysteroid dehydrogenase: partial purification of and evidence for a distinct NAD-dependent isoform. *Endocrinology* 132: 2614-2621.

Low SC, Assaad SN, Rajan V, Chapman KE, Edwards CRW and **Seckl JR** (1993). Regulation of 11ß-hydroxysteroid dehydrogenase by sex steroids in vivo: further evidence for the existence of a second dehydrogenase in rat kidney. *J Endocrinol* 139: 27-35.

Leckie C, Chapman KE, Edwards CRW and Seckl JR (1995). LLC-PK$_1$ cells model 11ß-hydroxysteroid dehydrogenase type 2 regulation of glucocorticoid access to renal mineralocorticoid receptors. *Endocrinology* 136: 5561-5569.

Rajan V, Edwards CRW, Seckl JR (1996). 11ß-hydroxysteroid dehydrogenase in cultured hippocampal cells reactivates inert 11-dehydrocorticosterone, potentiating neurotoxicity. *J Neuroscience* 16: 65-70.

Brown RW, Chapman KE, Edwards CRW and Seckl JR (1996). Purification of 11ß-hydroxysteroid dehydrogenase type 2 from human placenta. *Biochem J* 313: 997-1005

Brown RW, Kotolevtsev Y, Leckie C, Lindsay RS, Lyons V, Murad P, Mullins JJ, Chapman KE, Edwards CRW and Seckl JR (1996). Isolation and cloning of human placental 11ß-hydroxysteroid dehydrogenase-2 cDNA. *Biochem J* 313: 1007-1017

Brown RW, Diaz R, Robson AC, Kotolevtsev Y, Mullins JJ, Kaufman MH and Seckl JR (1996). The ontogeny of 11ß-hydroxysteroid dehydrogenase type 2 and mineralocorticoid receptor gene expression reveal intricate control of glucocorticoid action in development. *Endocrinol* 137: 794-797.

Voice M, Seckl JR and Chapman KE (1996). The sequence of 5'-flanking DNA from mouse 11ß-hydroxysteroid dehydrogenase type 1 and analysis of puative transcription factor binding sites. *Gene* 181: 233-235.

Lindsay RS, Lindsay RM, Edwards CRW and Seckl JR (1996). Inhibition of 11ß-hydroxysteroid dehydrogenase in pregnant rats and the programming of blood pressure in the offspring. *Hypertension* 27: 1200-1204.

Voice M, Seckl JR, Edwards CRW and Chapman KE (1996). 11ß-hydroxysteroid dehydrogenase type 1 expression in 2S-FAZA hepatoma cells is hormonally-regulated: a model for the study of hepatic corticosteroid metabolism. *Biochem J* 317: 621-625.

Waddell B, Benediktsson R and Seckl JR. (1996). 11ß-hydroxysteroid dehydrogenase type 2 in the rat corpus luteum: induction of mRNA expression and bioactivity coincident with luteal regression. *Endocrinology* 137: 5386-5391.

Lindsay RS, Lindsay RM, Waddell B and Seckl JR (1996). Programming of glucose tolerance in the rat: role of placental 11ß-hydroxysteroid dehydrogenase. *Diabetologia* 39: 1299-1305.

Rose KR, Stapleton G, Kieny M-P, Russell DW, Björkheim I, Seckl JR, Lathe R (1997). Cyp7b, a novel brain cytochrome P450, catalyses the synthesis of neurosteroids 7a-hydroxy DHEA and 7a-hydroxypregnenolone. *Proc Natl Acad Sci USA* 94: 4925-4930.

Kotolevtsev Y, Holmes MC, Burchell A, Houston PM, Schmoll D, Jamieson PM, Best R, Brown R, Edwards CRW, Seckl JR and Mullins JJ (1998). 11ß-hydroxysteroid dehydrogenase type 1 knockout mice show attenuated glucocorticoid inducible responses and resist hyperglycaemia on obesity or stress. *Proc Natl Acad Sci USA* 94: 14924-14929.

Diaz R, Brown R, Seckl JR (1998). Ontogeny of mRNAs encoding glucocorticoid and mineralocorticoid receptors and 11ß-HSDs in prenatal rat brain development reveal complex control of glucocorticoid action. *J Neurosci* 18: 2570-2580.

Napolitano A, Voice M, Edwards CRW, Seckl JR and Chapman KE (1998). 11ß-hydroxysteroid dehydrogenase type 1 in adipocytes: expression is differentiation-dependent and hormonally-regulated. *J Steroid Biochem Molec Biol* 64: 251-260.

Waddell B, Benediktsson R, Brown R and Seckl JR. (1998). Tissue-specific mRNA expression of 11B-hydroxysteroid dehydrogenase types 1 and 2 and the glucocorticoid receptor within rat placenta suggest exquisite local control of glucocorticoid action. *Endocrinology* 139: 1517-1523.

Nyirenda M, Lindsay RS, Kenyon CJ, Burchell A and Seckl JR (1998). Glucocorticoid exposure in late gestation permanently programmes rat hepatic phosphoenolpyruvate carboxykinase and glucocorticoid receptor expression and causes glucose intolerance in adult offspring. *J Clin Invest* 101: 2174-2181.

Robson AC, Leckie C, Seckl JR and Holmes MC (1998). Expression of 11ß-hydroxysteroid dehydrogenase type 2 in the postnatal and adult rat brain. *Molec Brain Res* 61: 1-10.

Jamieson PM, Chapman KE, Walker BR and Seckl JR (1999). Interactions between oestradiol and glucocorticoid regulatory effects on liver-specific glucocorticoid-inducible genes: possible evidence for a role of hepatic 11 beta-hydroxysteroid dehydrogenase type 1. *J Endocrinol* 160: 103-109.

Jamieson PM, Chapman KE and Seckl JR (1999). Tissue- and temporal-specific regulation of 11ß-hydroxysteroid dehydrogenase type 1 by glucocorticoids in vivo. *J Steroid Biochem Molec Biol* 68: 245-250.

Kotelevtsev Y, Brown RW, Fleming S, Kenyon CJ, Edwards CRW, Seckl JR and Mullins JJ (1999). Hypertension in mice lacking 11ß-hydroxysteroid dehydrogenase type 2. *J Clin Invest* 103: 683-689.

Meaney MJ, Diorio J, Francis D, Weaver S, Yau JLW, Chapman KE, Seckl JR (2000). Postnatal handling increases the expression of cAMP-inducible transcription factors in the rat hippocampus: The effects of thyroid hormones and serotonin. *J Neurosci* 20: 3926-35.

Welberg LAM, Seckl JR and Holmes MC (2000). Inhibition of 11ß-hydroxysteroid dehydrogenase, the feto-placental barrier to maternal glucocorticoids, permanently programs amygdala glucocorticoid receptor mRNA expression and anxiety-like behavior in the offspring. *Europ J Neurosci* 12: 1047-1054.

Jamieson PM, Chaman KE, Walker BR and Seckl JR (2000). 11ß-hydroxysteroid dehydrogenase type 1 is a predominant 11ß-reductase in the intact perfused rat liver. *J Endocrinol* 165: 685-692.

Williams LJS, Lyons V, MAcLeod I, Rajan V, Darlington GJ, Poli V, Seckl JR and Chapman KE (2000). C/EBP□ regulates hepatic transcription of 11ß-hydroxysteroid dehydrogenase type 1; a novel mechanisms for cross-talk between the C/EBP and glucocorticoid signalling pathways. *J Biol Chem* 275: 30232-30239.

Harris HJ, Kotelevtsev Y, Mullins JJ, Seckl JR and Holmes MC (2001). 11ß-hydroxysteroid dehydrogenase type 1 null mice have altered hypothalamic-pituitary-adrenal axis activity: a novel control of glucocorticoid feedback. *Endocrinology* 142: 114-120.

REVIEWS AND CHAPTERS

Seckl JR (1993). 11ß-HSD isoforms and their implications for blood pressure regulation. *Eur J Clin Invest* 23: 589-601.

Seckl JR and Brown RW (1994). 11ß-hydroxysteroid dehydrogenase: on several roads to hypertension. *J Hypertens* 12: 105-112.

Seckl JR and Olsson T (1995). Glucocorticoids and the age-impaired hippocampus: cause or effect? *J Endocrinol* 145: 201-211.

Yau JLW and Seckl JR (1995). Corticosteroids and the brain. *Curr Opin Endocrinol Diabetes*: 2: 239-247.

Edwards CRW, Benediktsson R, Lindsay RS and Seckl JR (1996). 11beta-hydroxysteroid dehydrogenases: Key enzymes in determining tissue-specific glucocorticoid effects. *Steroids* 61: 263-269.

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Chapman KE, Kotelevtsev YV, Jamieson PM, Williams LJS, Mullins JJ and Seckl JR (1997). Tissue-specific modulation of glucocorticoid action by the 11beta-hydroxysteroid dehydrogenases. *Biochem Soc Trans* 25: 583-587.

Seckl JR and Chapman KE (1997). Medical and physiological aspects of the 11ß-hydroxysteroid dehydrogenase system. *Eur J Biochem* 249: 361-364.

Seckl JR and Nyirenda MJ (1999). Glucocorticoids, feto-placental 11ß-hydroxysteroid dehydrogenase and the programming of hypertension. *Handbook of Hypertension* Vol. 19: Development of the Hypertensive Phenotype; McCarty R, Blizard DA, Chevalier RL (eds); Elsevier, Amsterdam, pp103-136.

Seckl JR (2000). 11ß-hydroysteroid dehydrogenases. *Encyclopaedia of Stress*. Fink G (ed). (in press).

Seckl JR and Walker BR (2001). 11ß-hydroxysteroid dehydrogenase type 1: a tissue-specific amplifier of glucocorticoid action. *Endocrinology* (in press).

Seckl JR and Walker BR (eds) (2001). Steroid Metabolism (book). *Bailliere's Clinical Endocrinology and Metabolism* (in press).